10/004,571R>

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
NEWS	4	OCT 28	KOREAPAT now available on STN
NEWS	5	NOV 30	PHAR reloaded with additional data
NEWS	6	DEC 01	LISA now available on STN
NEWS	7	DEC 09	12 databases to be removed from STN on December 31, 2004
NEWS	8	DEC 15	MEDLINE update schedule for December 2004
NEWS	9	DEC 17	ELCOM reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	10	DEC 17	COMPUAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	11	DEC 17	SOLIDSTATE reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	12	DEC 17	CERAB reloaded; updating to resume; current-awareness alerts (SDIs) affected
NEWS	13	DEC 17	THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB
NEWS	14	DEC 30	EPFULL: New patent full text database to be available on STN
NEWS	15	DEC 30	CAPLUS - PATENT COVERAGE EXPANDED
NEWS	16	JAN 03	No connect-hour charges in EPFULL during January and February 2005
NEWS	17	FEB 25	CA/CAPLUS - Russian Agency for Patents and Trademarks (ROSPATENT) added to list of core patent offices covered
NEWS	18	FEB 10	STN Patent Forums to be held in March 2005
NEWS	19	FEB 16	STN User Update to be held in conjunction with the 229th ACS National Meeting on March 13, 2005
NEWS	20	FEB 28	PATDPAFULL - New display fields provide for legal status data from INPADOC
NEWS	21	FEB 28	BABS - Current-awareness alerts (SDIs) available
NEWS	22	FEB 28	MEDLINE/LMEDLINE reloaded
NEWS	23	MAR 02	GBFULL: New full-text patent database on STN
NEWS	24	MAR 03	REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS	25	MAR 03	MEDLINE file segment of TOXCENTER reloaded

NEWS EXPRESS JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN

10/004,571R>

NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 17:05:55 ON 08 MAR 2005

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 17:06:01 ON 08 MAR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 6 MAR 2005 HIGHEST RN 843607-47-6
DICTIONARY FILE UPDATES: 6 MAR 2005 HIGHEST RN 843607-47-6

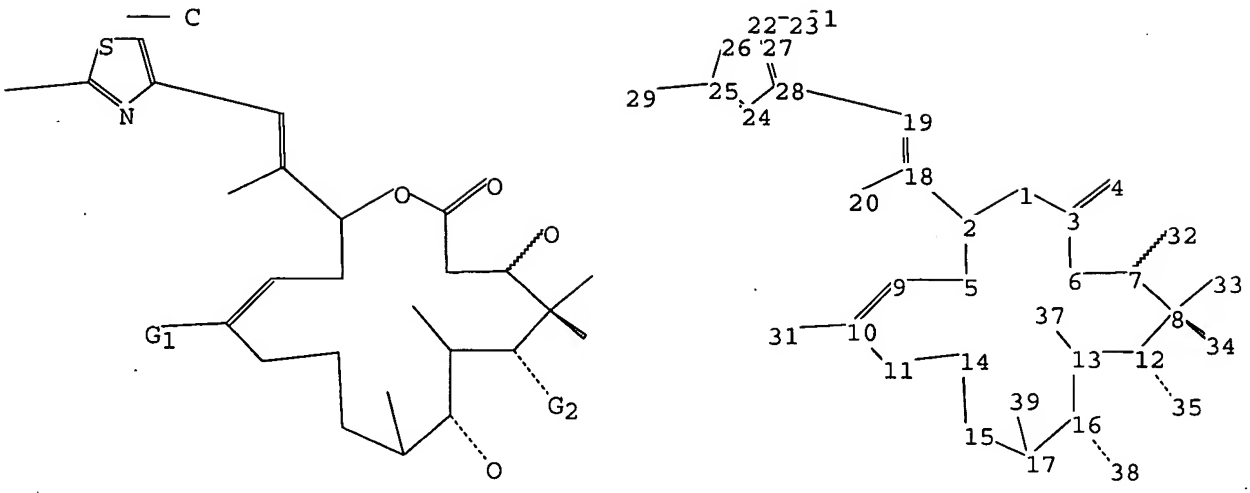
TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\10004571.str



chain nodes :
4 18 19 20 21 22 23 29 31 32 33 34 35 37 38 39
ring nodes :
1 2 3 5 6 7 8 9 10 11 12 13 14 15 16 17 24 25 26 27 28
chain bonds :
2-18 3-4 7-32 8-33 8-34 10-31 12-35 13-37 16-38 17-39 18-19 18-20 19-28
22-23 25-29
ring bonds :
1-2 1-3 2-5 3-6 5-9 6-7 7-8 8-12 9-10 10-11 11-14 12-13 13-16 14-15
15-17 16-17 24-25 24-28 25-26 26-27 27-28
exact/norm bonds :
3-4 7-32 10-31 12-35 16-38 24-25 24-28
exact bonds :
1-2 1-3 2-5 2-18 3-6 5-9 6-7 7-8 8-12 8-33 8-34 9-10 10-11 11-14
12-13 13-16 13-37 14-15 15-17 16-17 17-39 18-19 18-20 19-28 22-23 25-26
25-29 26-27 27-28
isolated ring systems :
containing 1 : 24 :

G1:H,Ak

G2:H,O

Match level :
1:Atom 2:Atom 3:Atom 4:CLASS 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:Atom 25:Atom 26:Atom 27:Atom 28:Atom
29:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS 35:CLASS 37:CLASS 38:CLASS
39:CLASS

Stereo Bonds:

34-8 (Single Hash).

Stereo Chiral Centers:

8 (Parity=Don't Care)

Stereo RSS Sets:

Type=Relative (Default). 1 Nodes= 8

L1 STRUCTURE UPLOADED

=> s l1
SAMPLE SEARCH INITIATED 17:06:29 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 68 TO ITERATE

100.0% PROCESSED 68 ITERATIONS (4 INCOMPLETE) 4 ANSWERS
SEARCH TIME: 00.00.01

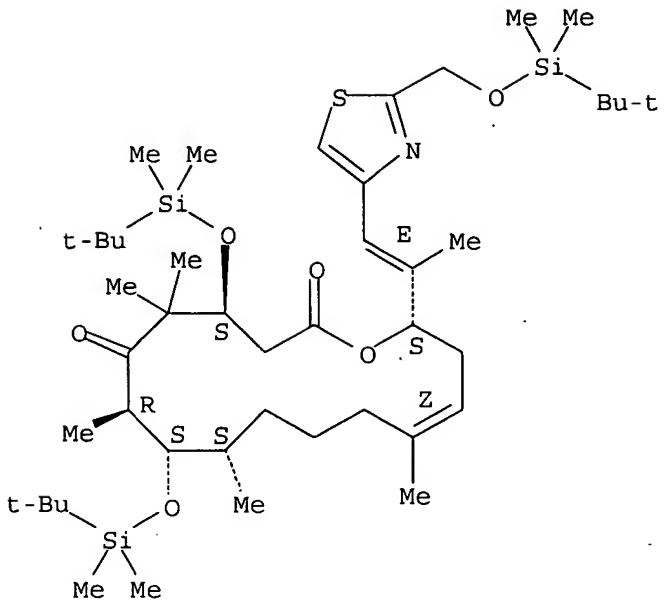
FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 866 TO 1854
PROJECTED ANSWERS: 4 TO 200

L2 4 SEA SSS SAM L1

=> d scan

L2 4 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
ITERATION INCOMPLETE
IN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-[(1E)-2-[2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-4-thiazolyl]-1-methylethenyl]-5,5,7,9,13-pentamethyl-, (4S,7R,8S,9S,13Z,16S)- (9CI)
MF C45 H83 N O6 S Si3

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

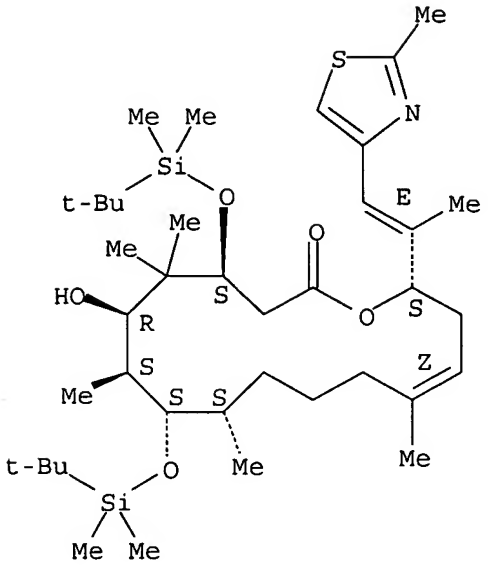


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):3

L2 4 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
ITERATION INCOMPLETE
IN Oxacyclohexadec-13-en-2-one, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-hydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,6R,7S,8S,9S,13Z,16S)- (9CI)
MF C39 H71 N O5 S Si2

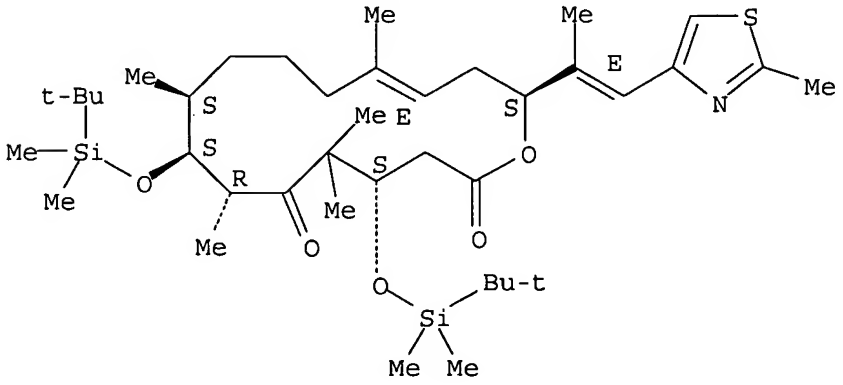
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 4 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
ITERATION INCOMPLETE
IN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI)
MF C39 H69 N O5 S Si2

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



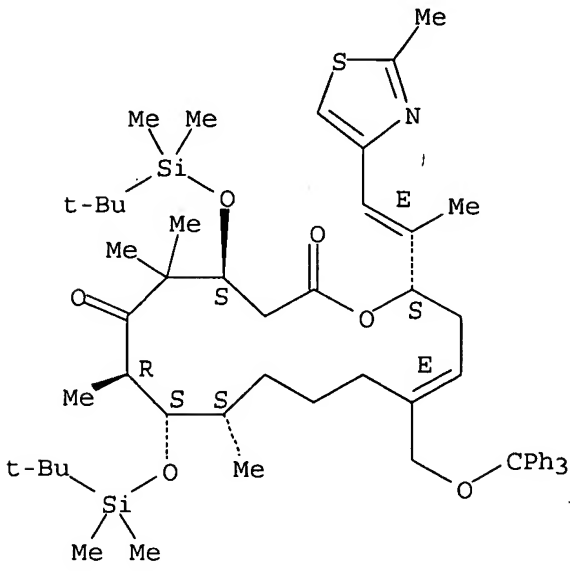
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 4 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
ITERATION INCOMPLETE
IN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-[(triphenylmethoxy)methyl]-, (4S,7R,8S,9S,13E,16S)- (9CI)

MF C58 H83 N O6 S Si2

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

=> s l1 ful
FULL SEARCH INITIATED 17:06:50 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 1517 TO ITERATE

100.0% PROCESSED 1517 ITERATIONS (80 INCOMPLETE) 80 ANSWERS
SEARCH TIME: 00.00.01

L3 80 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	161.76	161.97

FILE 'CAPLUS' ENTERED AT 17:06:59 ON 08 MAR 2005

FILE COVERS 1907 - 8 Mar 2005 VOL 142 ISS 11
FILE LAST UPDATED: 7 Mar 2005 (20050307/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s l3
L4          57 L3

=> s l4 (and process or prepar? or make or made or synthes?)
MISSING OPERATOR 'L4 (AND'
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l4 and (process or prepar? or make or made or synthes?)
       2057964 PROCESS
       1371858 PROCESSES
       3060581 PROCESS
                 (PROCESS OR PROCESSES)
       1532491 PREPAR?
        114913 PREP
          2021 PREPS
        116735 PREP
                 (PREP OR PREPS)
       1917417 PREPD
            21 PREPDS
       1917432 PREPD
                 (PREPD OR PREPDS)
        105866 PREPG
            12 PREPGS
        105877 PREPG
                 (PREPG OR PREPGS)
       2555437 PREPN
        198549 PREPNS
       2705847 PREPN
                 (PREPN OR PREPNS)
       4484517 PREPAR?
                 (PREPAR? OR PREP OR PREPD OR PREPG OR PREPN)
        205295 MAKE
        158542 MAKES
        353602 MAKE
                 (MAKE OR MAKES)
       1137640 MADE
            23 MADES
       1137660 MADE
                 (MADE OR MADES)
       1431845 SYNTHES?
L5          57 L4 AND (PROCESS OR PREPAR? OR MAKE OR MADE OR SYNTHES?)
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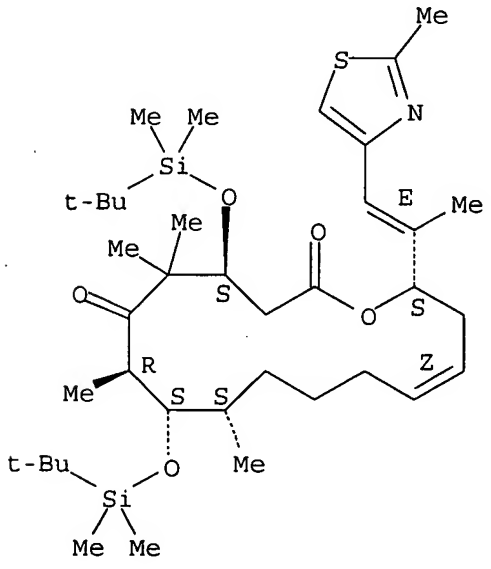
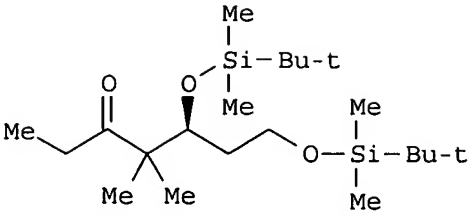
=> d l5 ibib hitstr abs 1-57

L5 ANSWER 1 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:454851 CAPLUS
DOCUMENT NUMBER: 141:140221
TITLE: Multi-step application of immobilized reagents and scavengers: A total **synthesis** of epothilone C
AUTHOR(S): Storer, R. Ian; Takemoto, Toshiyasu; Jackson, Philip S.; Brown, Dearg S.; Baxendale, Ian R.; Ley, Steven V.
CORPORATE SOURCE: Department of Chemistry, University of Cambridge, Cambridge, CB2 1EW, UK
SOURCE: Chemistry--A European Journal (2004), 10(10), 2529-2547
CODEN: CEUJED; ISSN: 0947-6539
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:140221
IT **186692-84-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total **synthesis** of epothilone C via asym. **synthesis** and stereoselective coupling of heptanone, methylheptenal, and thiazole fragments using immobilized reagents and scavengers)
RN 186692-84-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

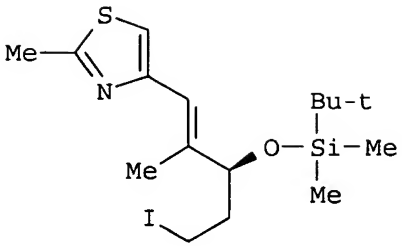
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



GI



I



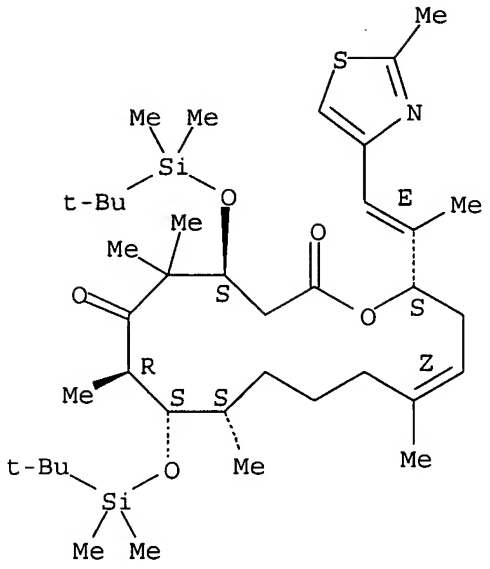
II

AB The total **synthesis** of the cytotoxic antitumor natural product epothilone C has provided a stage for the exploitation and further development of immobilized reagent methods. A stereoselective convergent synthetic strategy was applied, incorporating polymer-supported reagents, catalysts, scavengers and catch-and-release techniques to avoid frequent aqueous work-up and chromatog. purification The enantioselective **preparation** of 3 key fragments heptanone I, (S)-2-methyl-6-heptenal, and thiazole II along with their elaboration via diastereoselective coupling into epothilone C is presented.

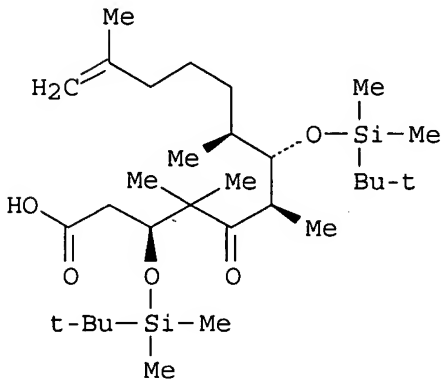
REFERENCE COUNT: 122 THERE ARE 122 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:106102 CAPLUS
DOCUMENT NUMBER: 140:357084
TITLE: Rapid access to epothilone analogs via semisynthetic degradation and reconstruction of epothilone D
AUTHOR(S): Dong, Steven D.; Sundermann, Kurt; Smith, Karen M. J.; Petryka, Joseph; Liu, Fenghua; Myles, David C.
CORPORATE SOURCE: Department of Chemistry, Kosan Biosciences, Hayward, CA, 94545, USA
SOURCE: Tetrahedron Letters (2004), 45(9), 1945-1947
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **189453-35-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**preparation** of epothilone D analogs via semisynthetic degradation and ring-closing metathesis and their antitumor activity)
RN 189453-35-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



GI



I

AB A facile and efficient route to epothilone analogs has been developed from the natural product epothilone D (I). Degradation of I via an oxidative cleavage sequence provides acid intermediate II rapidly in six steps. From II, a variety of epothilone analogs have been **prepared** utilizing ring-closing metathesis to reconstruct the trisubstituted-12,13-double bond. Using this approach, we report a number of epothilone analogs with varying C-15 aromatic side chains and C-14 allylic substitutions and their antitumor activities.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:986626 CAPLUS
DOCUMENT NUMBER: 141:379
TITLE: Conformation-activity relationships in polyketide natural products. Towards the biologically active conformation of epothilone

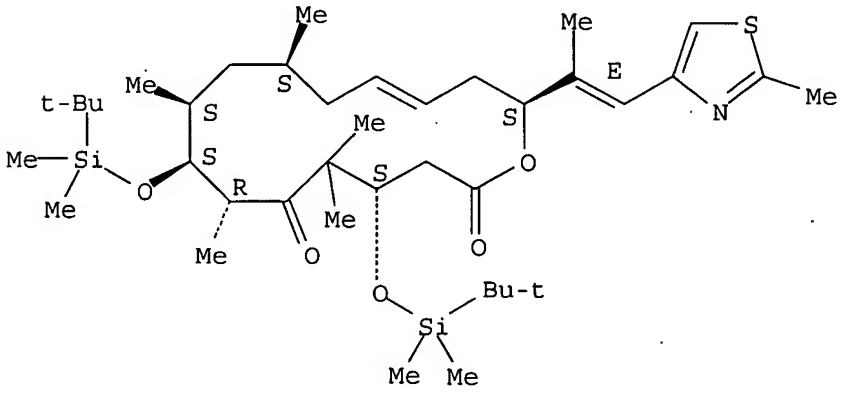
AUTHOR(S): Taylor, Richard E.; Chen, Yue; Galvin, Gabriel M.; Pabba, Praveen K.
CORPORATE SOURCE: Department of Chemistry & Biochemistry and the Walther Cancer Research Center, University of Notre Dame, Notre Dame, IN, 46556-5670, USA
SOURCE: Organic & Biomolecular Chemistry (2004), 2(1), 127-132
CODEN: OBCRAK; ISSN: 1477-0520
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:379

IT **746637-22-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(conformation-activity relationships in polyketide natural products reveals biol. active conformation of epothilone)

RN 746637-22-9 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,11-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,11S,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



AB The conformation-activity relationships for the biol. active polyketide, epothilone, have been determined Computer-based mol. modeling and high field NMR techniques have provided the solution preferences for epothilones 1 and 2. For the C1-C8 polypropionate region, two conformational families, conformers 1 and 2, have been identified as having significant populations in polar and non-polar solvents. In the C11-C15 region, addnl. flexibility was observed and two local conformations have been identified as important, conformers 3 and 4. Epothilone analogs with altered conformational profiles have been designed and **synthesized.** Conformational anal. and the results of biol. assays have been correlated to provide increased understanding of the biol. active conformation for the epothilone class of natural product. Conformation-activity relationships have been shown to be an important complement to structure-activity data.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

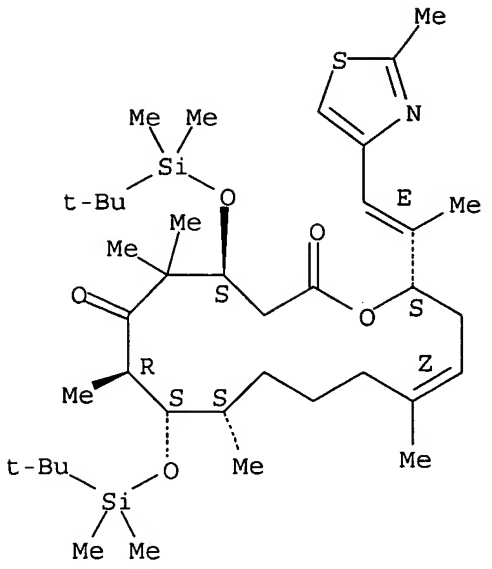
L5 ANSWER 4 OF 57 CAPLUS

ACCESSION NUMBER: 2003:434313 CAPLUS
DOCUMENT NUMBER: 139:22063
TITLE: **Preparation** of 14-methylepothilones for therapeutic use in treatment of cancer and other diseases or conditions characterized by cellular hyperproliferation
INVENTOR(S): Myles, David; Sundermann, Kurt; Dong, Steven
PATENT ASSIGNEE(S): Kosan Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

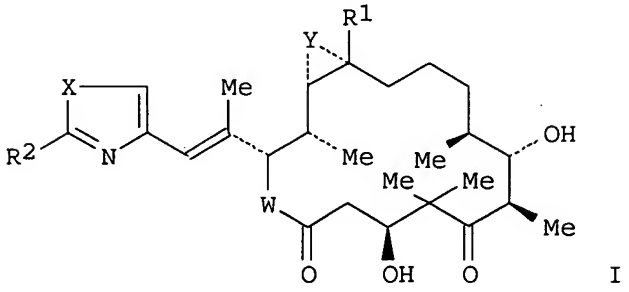
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003045324	A2	20030605	WO 2002-US37945	20021126
WO 2003045324	A3	20040415		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003134883	A1	20030717	US 2002-304315	20021126
PRIORITY APPLN. INFO.:			US 2001-333465P P	20011126

OTHER SOURCE(S): MARPAT 139:22063
IT **189453-35-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**preparation** of 14-methylepothilones for therapeutic use in treatment of cancer and other diseases and conditions characterized by undesired cellular hyperproliferation)
RN 189453-35-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



GI



I

AB 14-Methylepothilone compds., such as I [R1 = H, alkyl; R2 = CH2OH, CH2NH2, alkyl; W = O, NH; X = S, O; Y = O, bond], were **prepared** for use in treatment of cancer and other diseases and conditions characterized by undesired cellular hyperproliferation. Thus, (14S)-14-Methylepothilone D I (R1 = R2 = Me, W = O, X = S, Y = bond) was **prepared** via a multistep synthetic sequence which included a metathesis/macrocyclization step. The **prepared** 14-methylepothilones were assayed for activity against several cell lines, such as MCF-7, NCI-ADR and H460.

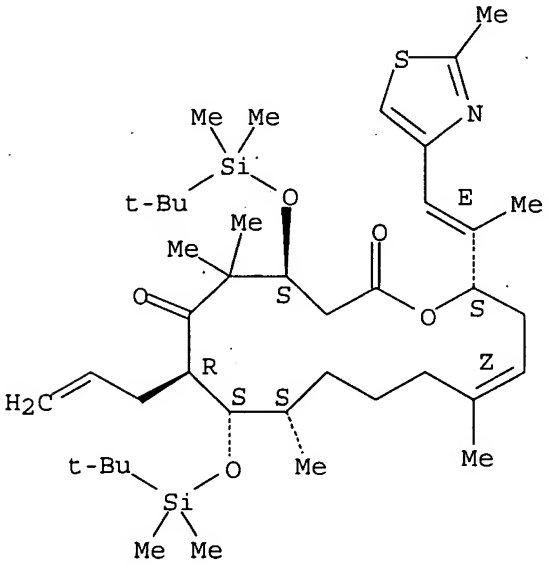
L5 ANSWER 15 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:157050 CAPLUS
DOCUMENT NUMBER: 136:216592
TITLE: Procedures for the production of 12,13-cyclopropylepothilone derivatives, as well as for their use in pharmaceutical **preparations**
PATENT ASSIGNEE(S): Schering Ag, Germany
SOURCE: Ger. Offen., 64 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent

LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10041470	A1	20020228	DE 2000-10041470	20000818

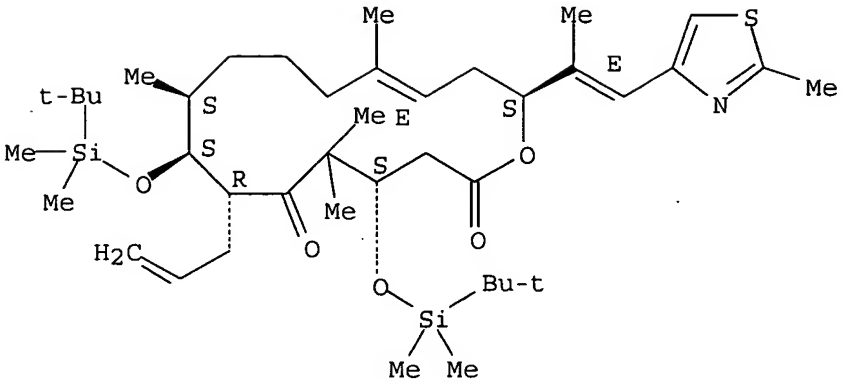
PRIORITY APPLN. INFO.: DE 2000-10041470 20000818
OTHER SOURCE(S): CASREACT 136:216592; MARPAT 136:216592
IT **305840-23-7P 305840-28-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**preparation** of 12,13-cyclopropylepothilone derivs. and their use in pharmaceutical compns.)
RN 305840-23-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,9,13-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-7-(2-propenyl)-, (4S,7R,8S,9S,13Z,16S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

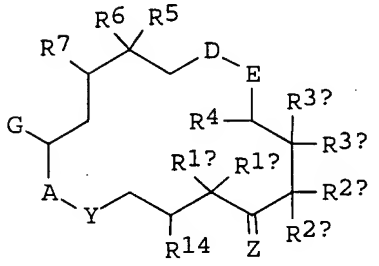


RN 305840-28-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,9,13-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-7-(2-propenyl)-, (4S,7R,8S,9S,13E,16S)-(9CI) (CA INDEX NAME)

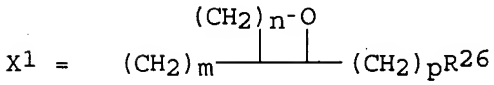
Absolute stereochemistry.
Double bond geometry as shown.

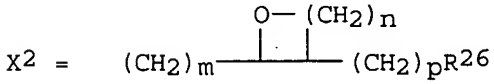


GI



I



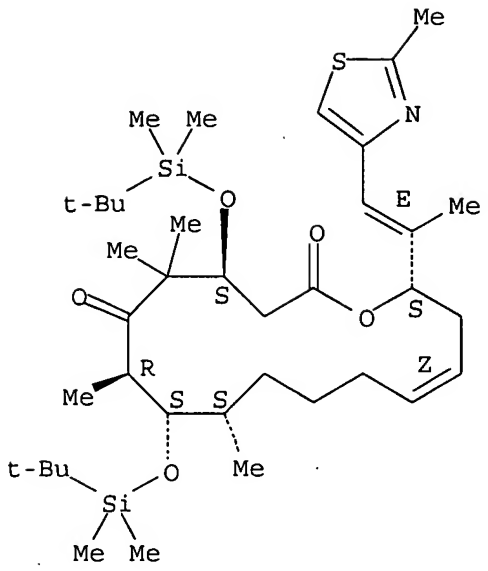


AB The present invention describes new 6-alkenyl- and 6-alkynylepothilone derivs., e.g., I [R1a, R1b = H, C1-10-alkyl, aryl, C7-20-aralkyl; R1aR1b = (CH2)r, CH2OCH2; r = 1 - 5; R2a = H, C1-10-alkyl, aryl, C7-20-aralkyl, (CH2)m-C.tplbond.C-(CH2)pR26, (CH2)m-C:C-(CH2)pR26, X1, X2; n = 0 - 5; p = 0 - 3; m = 0 - 4; R2b = (CH2)m-C.tplbond.C-(CH2)pR26, (CH2)m-C:C-(CH2)pR26, X1, X2; R3a = H, C1-10-alkyl, aryl, C7-20-aralkyl; R3b = O-protecting group; R4 = H, C1-10-alkyl, aryl, C7-20-aralkyl, halogen, OH, O-protecting group, CN; R5 = H, C1-10-alkyl, aryl, C7-20-aralkyl, (CH2)s-T; S = 1 - 4; T = OH, O-protecting group, halogen; R6R7 = C(R33)2, NR32 AY = OC(:O), OCH2, CH2C(:O), NR29C(:O), NR29SO2; DE = CH2CH2, CH2O, OCH2; G = X:CR8-, bicyclic or tricyclic aryl; X = O, (O-alkyl)2, etc.; Z = H, H,OH, H,O-protective group; R8 = H, halogen, CN, C1-20-alkyl, aryl, C7-20-aralkyl; R14 = H, OH, halogen, O-SO2-alkyl, O-SO2-aryl, O-SO2-aralkyl; R26 = H, C1-10-alkyl, aryl, C7-20-aralkyl, C1-10-acyl, OH,

O-protecting group; R29 = H, C1-20-alkyl; R32 = H, C1-4-alkyl, C1-4-acyl; R33 = H, halogen], which interact with tubulins by stabilizing the formed microtubulins (no data). I are able specifically to affect cell division and are suitable, for example for the treatment of malignant tumors ovarial -, stomach -, colon -, adeno -, chest -, lungs -, head and neck carcinoma, malignant melanoma, acute lymphocytic and myelocytic leukemia. In addition I are suitable for the anti-angiogenesis therapy as well as for the treatment of chronic ignitable illnesses (psoriasis, arthritis). For the avoidance of uncontrolled cell rampant growths on as well as the better compatibility of medical implants I can be up and/or brought into polymers materials. According to invention, I can be used alone or for the achievement of additive or synergistic effects in combination with further principles and substance classes applicable in the tumor therapy. Exptl. data from patents PCT/EP00/01333 and PCT/IB00/00657 are reproduced here.

L5 ANSWER 16 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:11427 CAPLUS
DOCUMENT NUMBER: 136:279243
TITLE: Alkyne metathesis: development of a novel molybdenum-based catalyst system and its application to the total **synthesis** of epothilone A and C
AUTHOR(S): Furstner, Alois; Mathes, Christian; Lehmann, Christian W.
CORPORATE SOURCE: Max-Planck-Institut fur Kohlenforschung, Mulheim/Ruhr, 45470, Germany
SOURCE: Chemistry--A European Journal (2001), 7(24), 5299-5317 CODEN: CEUJED; ISSN: 0947-6539
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:279243
IT **186692-84-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(alkyne metathesis, development of a novel molybdenum-based catalyst system and its application to the total **synthesis** of epothilone A and C)
RN 186692-84-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Sterically hindered molybdenum(III) amido complexes of the general type [Mo{(tBu)(Ar)N}3], e.g. I, upon treatment with CH2Cl2 or other halogen donors, have been converted into highly effective catalysts for all kinds of alkyne metathesis reactions. Although the actual nature of the propagating species formed in situ is still elusive, halogen transfer to the Mo center of I plays a decisive role in the activation of such precatalysts. It was possible to isolate and characterize by X-ray crystallog. some of the resulting molybdenum halide derivs. such as II (R = OMe, X = Cl), II (R = Me, X = Cl) and III which themselves were shown to be catalytically active. Numerous applications illustrate the performance of the catalytic system I/CH2Cl2 which operates under mild conditions and tolerates an array of polar functional groups. The wide scope allows the method to be implemented into the total **synthesis** of sensitive and polyfunctional natural products. Most notable among them is a concise entry into the potent anticancer agents epothilone A and C. The macrolide core of these targets is forged by ring closing alkyne metathesis (RCAM) of diyne IV, followed by Lindlar hydrogenation of the resultant cycloalkyne thus formed. Since this strategy opens a stereoselective entry into (Z)-alkene V, the approach is inherently more efficient than previous **syntheses** based on conventional RCM.

REFERENCE COUNT: 169 THERE ARE 169 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 26 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:138738 CAPLUS
DOCUMENT NUMBER: 134:311010
TITLE: Synthetic epothilone analogs with modifications in the

northern hemisphere and the heterocyclic side-chain-**synthesis** and biological evaluation

AUTHOR(S): End, Nicole; Bold, Guido; Caravatti, Giorgio; Wartmann, Markus; Altmann, Karl-Heinz

CORPORATE SOURCE: TA Oncology Research, Novartis Pharma AG, Basel, CH-4002, Switz.

SOURCE: Proceedings of ECSOC-3, [and] Proceedings of ECSOC-4, Sept. 1-30, 1999 and 2000 (2000), Meeting Date 1999-2000, 1431-1442. Editor(s): Pombo-Villar, Esteban. Molecular Diversity Preservation International: Basel, Switz. CODEN: 69AXZT

DOCUMENT TYPE: Conference; (computer optical disk)

LANGUAGE: English

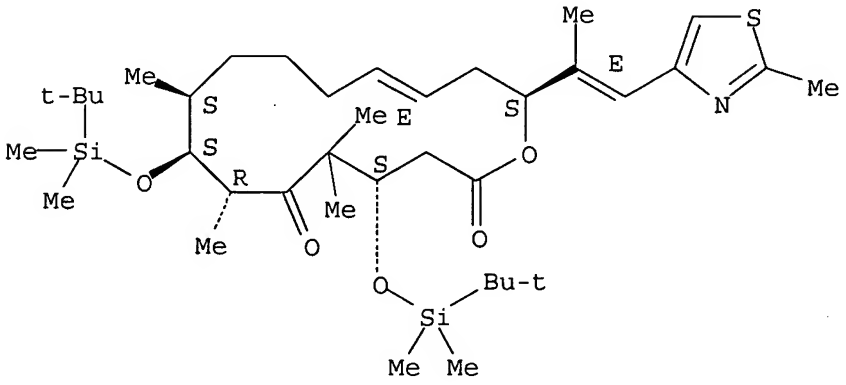
OTHER SOURCE(S): CASREACT 134:311010

IT **188260-22-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthetic epothilone analogs with modifications in the northern hemisphere and the heterocyclic side-chain-**synthesis** and biol. evaluation)

RN 188260-22-2 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



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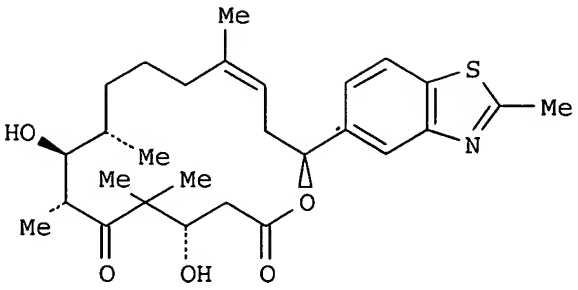


I

AB The authors have **synthesized** epothilone analogs, e.g. I, with modifications in the northern hemisphere and the heterocyclic side-chain. In all three cases the key steps for construction of the macrocyclic skeleton involve Yamaguchi macrolactonization, the build-up of the requisite seco-acid through aldol reaction between the C7-C15 aldehyde and the dianion of the O-protected C1-C6 β-hydroxy acid fragment, and the assembly of the C7-C15 aldehyde through the appropriate type of Pd(0)-catalyzed coupling reaction. The IC50 for growth inhibition of the KB-31 tumor cell line for I was 0.45 nM.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 33 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:254124 CAPLUS
DOCUMENT NUMBER: 132:293600
TITLE: An efficient procedure for the **synthesis** of epothilone B, derivatives, and its intermediates
INVENTOR(S): Mulzer, Johann; Mantoulidis, Andreas; Oehler, Elisabeth
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Ger. Offen., 32 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19848306	A1	20000420	DE 1998-19848306	19981014
CA 2346493	AA	20000427	CA 1999-2346493	19991014
WO 2000023452	A1	20000427	WO 1999-EP7746	19991014
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9964717	A1	20000508	AU 1999-64717	19991014
AU 763717	B2	20030731		
EP 1121364	A1	20010808	EP 1999-952569	19991014

EP 1121364	B1	20030108			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
JP 2002527521	T2	20020827	JP 2000-577178		19991014
AT 230751	E	20030115	AT 1999-952569		19991014
PT 1121364	T	20030430	PT 1999-952569		19991014
ES 2189508	T3	20030701	ES 1999-952569		19991014
US 6605726	B1	20030812	US 2001-807370		20010601
US 2003220503	A1	20031127	US 2003-420716		20030423
PRIORITY APPLN. INFO.:			DE 1998-19848306	A	19981014
			WO 1999-EP7746	W	19991014
			US 2001-807370	A3	20010601

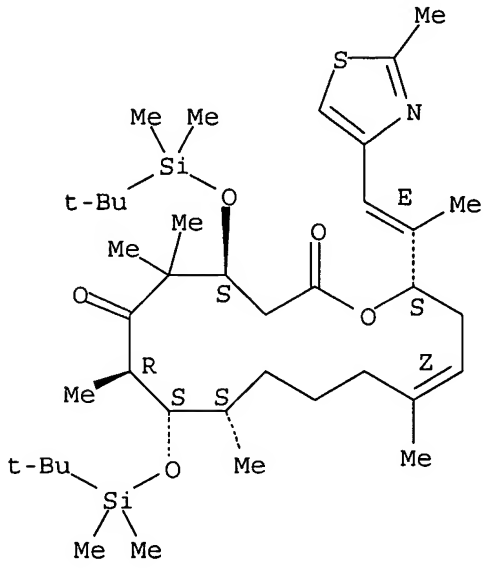
OTHER SOURCE(S): CASREACT 132:293600; MARPAT 132:293600

IT **189453-35-8P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**synthesis** of epothilone B, derivs., and its intermediates)

RN 189453-35-8 CAPLUS

CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



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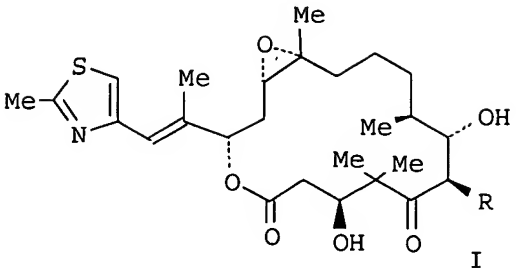

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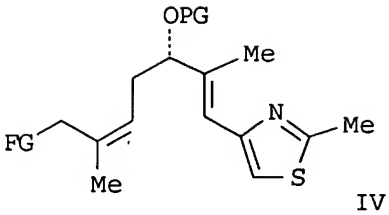


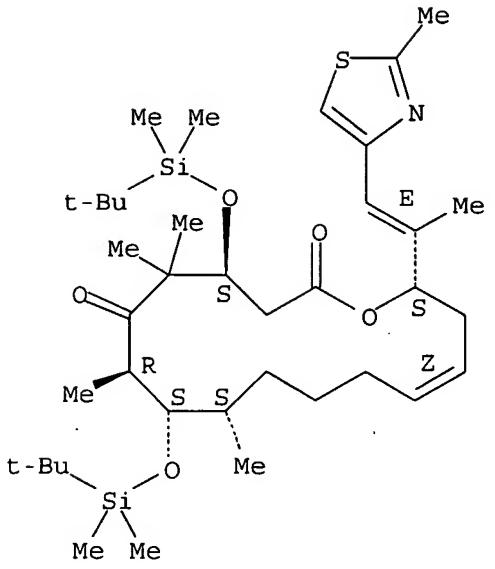
IV

AB A new procedure for the production of epothilone B and its derivs. (I) (R = alkyl, cycloalkyl, aryl, heteroaryl, methylaryl, etc.) including its intermediates is reported. The method is based upon the stereoselective **synthesis** of three key structural fragments, C1-C6 (II) (S)-PGO(CH2)2CH(OPG)CMe2COCH2R, C7-C10 (III) (S)-PGOCH2CH(Me)CH2CH2FG, (PG = hydroxyl protecting group, such as TBDMS, etc. ; FG = SO2Ph, I, etc.), and C11-C20 (IV) starting with D-valine, TBDPS protected (2S)-methylpropan-1,3-diol and (S)-3-hydroxybutyrolactone, resp. The product, obtained after coupling of III and IV, on reaction with II formed an intermediate which on macrocyclization produced I.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 34 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:52387 CAPLUS
DOCUMENT NUMBER: 132:251011
TITLE: Enantioselective total **synthesis** of epothilone A using multifunctional asymmetric catalyses
AUTHOR(S): Sawada, Daisuke; Shibasaki, Masakatsu
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, The University of Tokyo, Tokyo, 113-0033, Japan
SOURCE: Angewandte Chemie, International Edition (2000), 39(1), 209-213
CODEN: ACIEF5; ISSN: 1433-7851
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 132:251011
IT **186692-84-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(enantioselective total **synthesis** of epothilone A)
RN 186692-84-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



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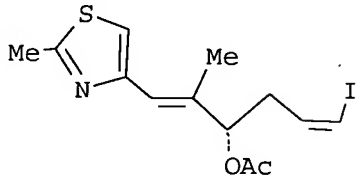

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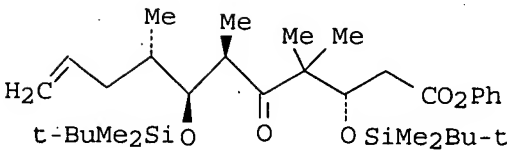
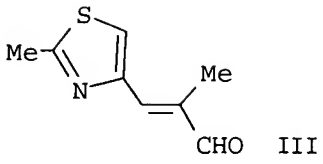


II



III

AB The enantioselective total **synthesis** of epothilone A was achieved via the catalytic coupling of I and II. The key step in the **preparation** of I was the catalytic cyanosilylation of III. II was **prepared** via a catalytic organic acetalization followed by an aldol reaction.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 35 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:15195 CAPLUS
DOCUMENT NUMBER: 132:64110
TITLE: The **preparation process**, intermediate products and pharmaceutical use of epothilone derivatives

INVENTOR(S): Buchmann, Bernd; Klar, Ulrich; Skuballa, Werner; Schwede, Wolfgang; Schirner, Michael; Menrad, Andreas
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000000485	A1	20000106	WO 1999-EP4915	19990630
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19830060	A1	20000210	DE 1998-19830060	19980630
DE 19923001	A1	20001116	DE 1999-19923001	19990513
AU 9950369	A1	20000117	AU 1999-50369	19990630

PRIORITY APPLN. INFO.:

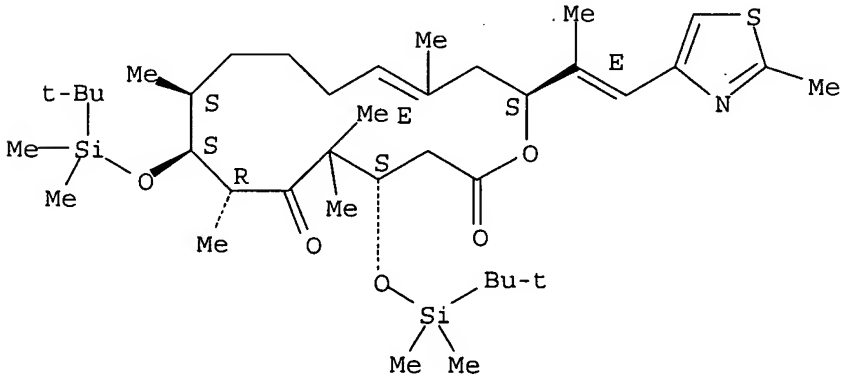
DE 1998-19830060	A	19980630
DE 1999-19923001	A	19990513
WO 1999-EP4915	W	19990630

OTHER SOURCE(S): CASREACT 132:64110; MARPAT 132:64110

IT **253448-16-7P 253448-18-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**preparation** and pharmaceutical use of epothilone derivs.)

RN 253448-16-7 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,14-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13E,16S)- (9CI) (CA INDEX NAME)

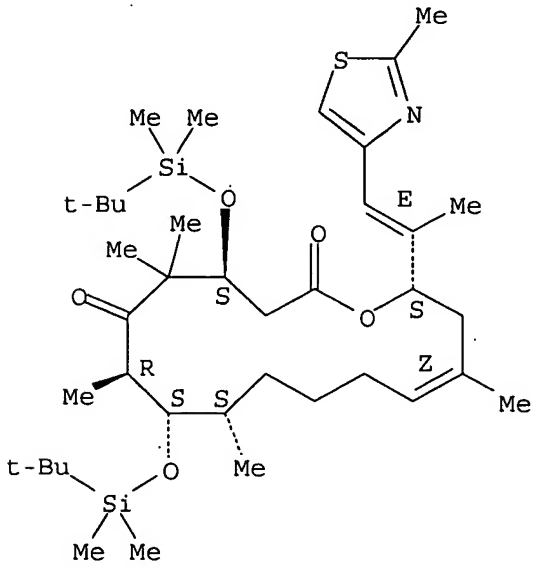
Absolute stereochemistry.
Double bond geometry as described by E or Z.



RN 253448-18-9 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,14-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to new epothilone derivs. I [R1a, R1b = H, C1-10-alkyl, aryl, C7-10-aralkyl; R1aR1b = (CH2)m, m = 2 - 5; R2a, R2b = H, C1-10-alkyl, aryl, C7-10-aralkyl; R2aR2b = (CH2)n, n = 2 - 5; R3 = H, C1-10-alkyl, aryl, C7-10-aralkyl; R4a, R4b = H, C1-10-alkyl, aryl, C7-10-aralkyl; R4aR4b = (CH2)m, m = 2 - 5; D-E = CH2CH2, CH:CH, C.tplbond.C, oxirane ring, CH(OH)CH(OH), CH(OH)CH2; R5 = C1-10-alkyl, aryl, C7-10-aralkyl; R6, R7 = H; R6R7 = O, bond; R8 = C1-10-alkyl, aryl, C7-10-aralkyl; R25 = H, C1-10-alkyl, C1-10-hydroxyalkyl, C1-10-haloalkyl; X = O, (OR9)2, C2-10-alkylene-α,ω-dioxy, CR11R12; CX = CH(OR10); R9 = C1-20-alkyl; R10 = H, protecting group; R11, R12 = H, C1-10-alkyl, aryl, C7-10-aralkyl; R11R12 = CH2, C5-7-carbocyclic ring; Y = O, CY = CH2; CZ = CH(OR13), R13 = H, protecting group] which are **prepared** via cyclization of ketones II [R15 = H, OH halogen, OR15a, OSO2R15b; R15a = H, SO2-alkyl, SO2-aryl, SO2-aralkyl, (CH2)o, CR16aR16b; R15b = H, C1-20-alkyl, aryl, C7-20-aralkyl; R16a, R16b = H, C1-10-alkyl, aryl, C7-20-aralkyl; R16aR16b = (CH2)q; o = 2 - 4; q = 3 - 6]. Thus, epothilone derivative III was **prepared** via macrolactonization of carboxylic acid IV with 2,4,6-trichlorobenzoyl chloride and Et3N in THF followed by deprotection with aqueous CF3CO2H in CH2Cl2. I cooperate with tubulin by stabilizing formed microtubuli.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 36 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:691091 CAPLUS
DOCUMENT NUMBER: 131:310502
TITLE: **synthesis** and cytotoxicity of 12,13-modified epothilone derivatives for use in treatment of tumors or other hyperproliferative cellular disease
INVENTOR(S): Vite, Gregory D.; Kim, Soong-Hoon Kim; Hofle, Gerhard
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9954319	A1	19991028	WO 1999-US7475	19990405
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG				
US 6380395	B1	20020430	US 1999-280192	19990329
US 6399638	B1	20020604	US 1999-280191	19990329
CA 2329181	AA	19991028	CA 1999-2329181	19990405
AU 9934716	A1	19991108	AU 1999-34716	19990405
AU 748526	B2	20020606		
BR 9909795	A	20001226	BR 1999-9795	19990405
TR 200003036	T2	20010122	TR 2000-200003036	19990405
EP 1073648	A1	20010207	EP 1999-916383	19990405
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002512239	T2	20020423	JP 2000-544658	19990405

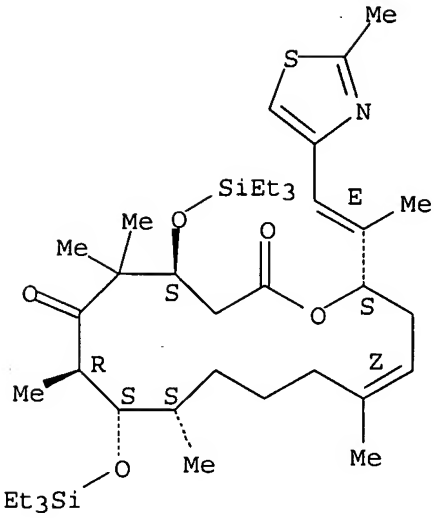
PRIORITY APPLN. INFO.: US 1998-82564P P 19980421
WO 1999-US7475 W 19990405

OTHER SOURCE(S): MARPAT 131:310502

IT **247230-54-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**synthesis** and cytotoxicity of 12,13-modified epothilone derivs. for use in treatment of tumors or other hyperproliferative cellular disease)

RN 247230-54-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,8-bis[(triethylsilyl)oxy]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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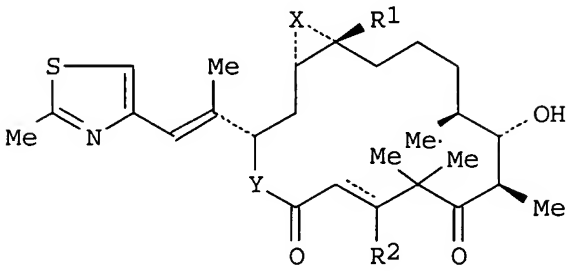


I

AB **Synthesis** and cytotoxicity of 12,13-modified epothilone derivs. (I) [R1 = H, (un)substituted alkyl; R2 = H if bond double or βOH if bond single; Y = O, NH; X = O, (un)substituted NH, OCH2, 2-methylthiazolo, S, (un)substituted CH2] is presented. Thus, I (R1 = H, X = NH, R2 = βOH, Y = O) (II) is **prepared** by epoxidn. of epothilone C followed by azidation and reductive imination. I are useful in treatment of tumors or other hyperproliferative cellular disease and show IC50 of 0.01-1000 nM in cell proliferation tests.

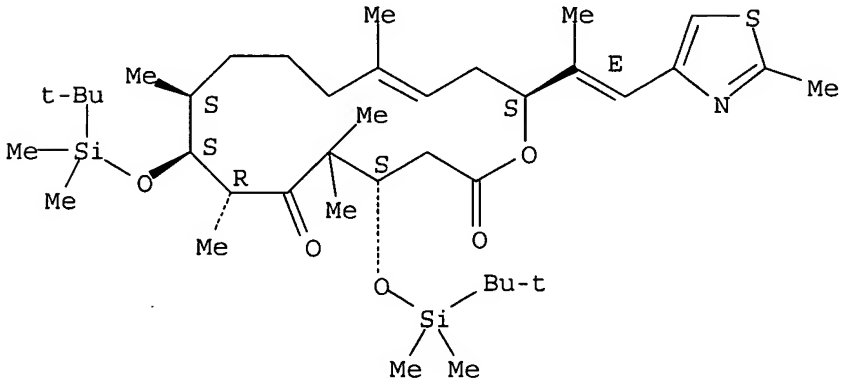
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 45 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:492150 CAPLUS
DOCUMENT NUMBER: 129:216449
TITLE: Total **synthesis** of (-)-epothilone B
AUTHOR(S): May, Scott A.; Grieco, Paul A.
CORPORATE SOURCE: Department of Chemistry and Biochemistry, Montana State University, Bozeman, MT, 59717, USA
SOURCE: Chemical Communications (Cambridge) (1998), (15), 1597-1598
CODEN: CHCOFS; ISSN: 1359-7345
PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal
LANGUAGE: English
IT **204195-20-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total **synthesis** of (-)-epothilone B)
RN 204195-20-0 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as described by E or Z.



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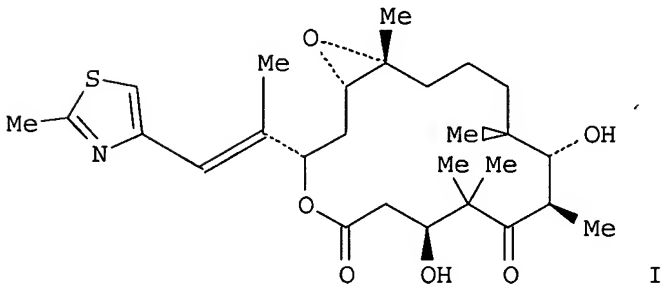

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AB The sixteen-membered ring macrolide (-)-epothilone B (I) has been **synthesized** by a route which features stereospecific methylation of an (E)-γ,δ-epoxy acrylate, the use of a double asym. reaction employing (R,R)-diisopropyltartrate and (E)-crotylboronate, ring closure by means of an olefin metathesis reaction.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

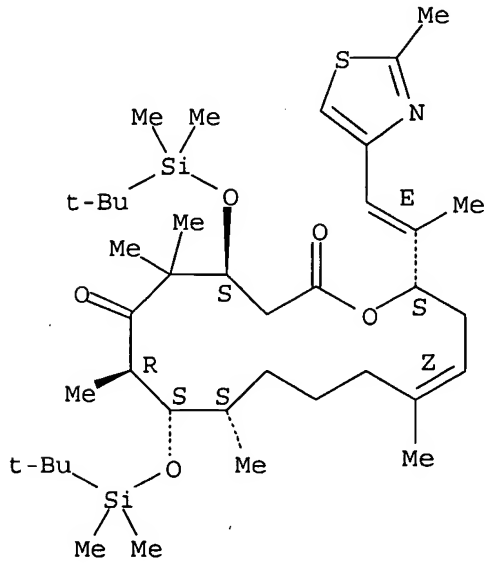
L5 ANSWER 53 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:302059 CAPLUS

DOCUMENT NUMBER: 127:4948
TITLE: Total **synthesis** of (-)-epothilone B: an extension of the Suzuki coupling method and insights into structure-activity relationships of the epothilones
AUTHOR(S): Su, Dai-Shi; Meng, Dongfang; Bertinato, Peter; Balog, Aaron; Sorensen, Erik J.; Danishefsky, Samuel J.; Zheng, Yu-Huang; Chou, Ting-Chao; He, Lifeng; Horwitz, Susan B.
CORPORATE SOURCE: Laboratory for Bioorganic Chemistry, Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SOURCE: Angewandte Chemie, International Edition in English (1997), 36(7), 757-759
CODEN: ACIEAY; ISSN: 0570-0833
PUBLISHER: VCH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 127:4948

IT **189453-35-8P 189453-54-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**synthesis** of epothilone B via a Suzuki coupling and insights into antitumor structure-activity relationships)

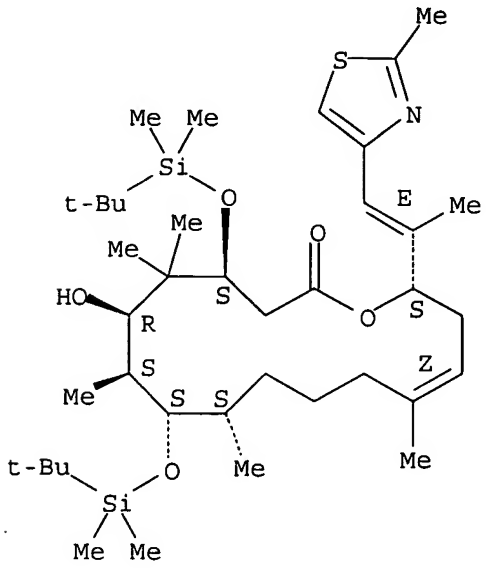
RN 189453-35-8 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 189453-54-1 CAPLUS
CN Oxacyclohexadec-13-en-2-one, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-hydroxy-5,5,7,9,13-pentamethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,6R,7S,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



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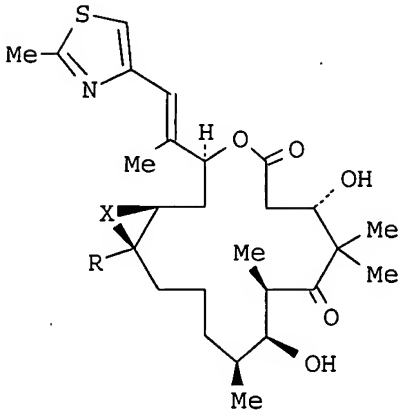

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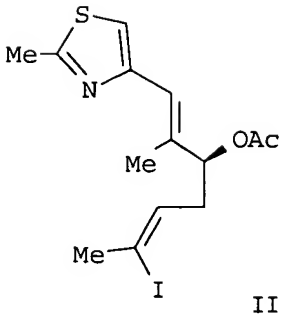

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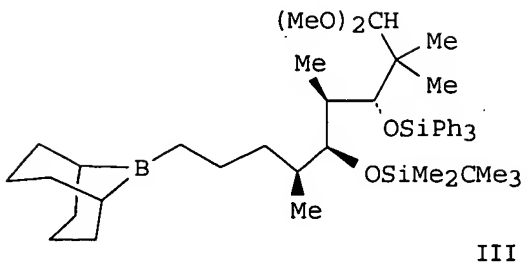


III

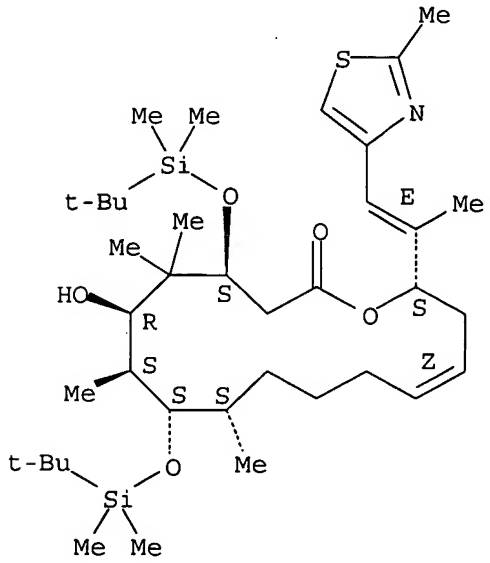
AB (-)-Epothilone B (I; R = Me, X = O) and desoxyepothilone B (I; R = Me, X =

bond) were **prepared** via Suzuki coupling of (Z)-vinyl iodide II with borane III. I (R = H, Me, X = O, bond) and the E-isomers of I (R = H, Me, X = bond) were tested for efficacy against drug-sensitive and resistant CCRF-CEM cell lines (IC50 = 0.0004 - 0.262 μM).

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

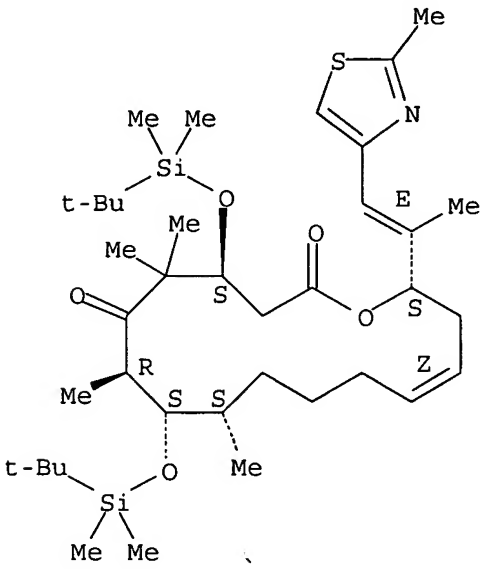
L5 ANSWER 57 OF 57 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:72321 CAPLUS
DOCUMENT NUMBER: 126:144023
TITLE: Total **synthesis** of (-)-epothilone A
AUTHOR(S): Balog, Aaron; Meng, Dongfang; Kamenecka, Ted; Bertinato, Peter; Su, Dai-Shi; Sorensen, Erik J.; Danishefsky, Samuel J.
CORPORATE SOURCE: Lab. for Bioorganic Chemistry, Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SOURCE: Angewandte Chemie, International Edition in English (1997), Volume Date 1996, 35(23/24), 2801-2803
CODEN: ACIEAY; ISSN: 0570-0833
PUBLISHER: VCH
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **186692-83-1P 186692-84-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total **synthesis** of (-)-epothilone A via a B-alkyl Suzuki coupling followed by closure of the macrocycle with an aldol reaction)
RN 186692-83-1 CAPLUS
CN Oxacyclohexadec-13-en-2-one, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-hydroxy-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,6R,7S,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 186692-84-2 CAPLUS
CN Oxacyclohexadec-13-ene-2,6-dione, 4,8-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5,7,9-tetramethyl-16-[(1E)-1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-, (4S,7R,8S,9S,13Z,16S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



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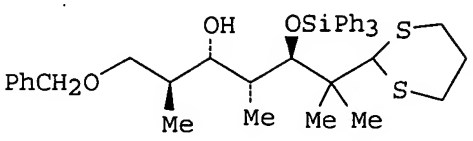

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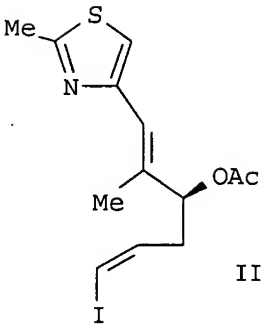
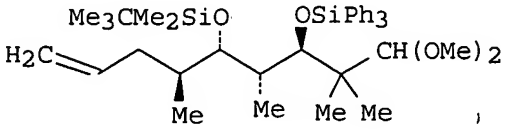


II



III

AB (-)-Epothilone A was **prepared** from dithiane I, (R)-glycidol and [(2-methyl-1,3-thiazol-4-yl)methyl]diphenylphosphine oxide via a B-alkyl Suzuki coupling of thiazole II with acetal III followed by closure of the macrocycle with an aldol reaction.
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-41.61	-41.61

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